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2.

FIBRINOUS OR MEMBRANOUS RHINITIS

AND ITS

RELATION TO DIPHTHERIA

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This interesting affection has attracted attention in recent years, especially in Germany and America; but, although it is by no means uncommon, little has been written on it in this country. The older observers were of the opinion that the affection was entirely distinct from diphtheria, whilst recent observers, relying chiefly on the results of bacteriological examination, have asserted the identity of the two diseases.

During the past fifteen months (ending October, 1897) I have examined clinically and bacteriologically thirty-six cases of this affection, and have especially endeavoured to trace its connection with diphtheria. This investigation seemed to me important, as it might possibly throw light

on some of the bacteriological problems connected with diphtheria, and also discover a possible overlooked source of diphtheritic infection. The disease seems to be very common. Sixteen cases occurred at the Children's Hospital, Paddington Green, in one year, out of a total of seven hundred new cases,—that is, they formed about $2\frac{1}{4}$ per cent. of the patients seen. Many other observers have also published series of cases, and, as will appear later, many cases probably do not apply for treatment at all, or if they do, pass unrecognised by well-qualified observers.

Fibrinous rhinitis may be defined as a subacute or chronic affection of the nose, characterised by the formation of a fibrinous, membranous, or shreddy exudation on the nasal mucous membrane.

The affection occurs most commonly in young children, and commences with the ordinary symptoms of catching cold. The nose becomes stopped up, may appear a little red and swollen, and there is a more or less profuse watery discharge. The child may be a little feverish, or complain of headache, seem tired or languid, lose appetite, &c., for the first day or two, but is not sufficiently ill to lie up. As a rule, indeed, it plays about or attends school as usual, and the constitutional disturbance when present at the commencement never persists for more than a day or two. The nasal obstruction and discharge continue, and the latter after a week or so often becomes of a more purulent character. When unilateral such symptoms closely resemble those of a foreign body in the nose, for which the affection is often mistaken. It is for these symptoms, when they have persisted two or three weeks, that relief is usually sought.

On examination there is seen to be complete bilateral or unilateral nasal obstruction, accompanied by a clear watery or muco-purulent discharge, with sometimes more or less irritation of the nostrils and upper lip, or even extensive impetigo.

Fibrinous exudation can be seen over the mucous

membrane of the affected nostril, and sometimes large loose pieces of membrane can be removed with forceps. The general health always seems good, and remains so throughout. The affection lasts on the average four to eight weeks or more, and apparently leaves no sequelæ. Briefly the symptoms are those of a more or less severe cold in the head, and only attract attention from their persistence.

Primary nasal diphtheria has long been recognised, and was well described by Bretonneau. Schuller in 1871, in the case of an infant dying of erysipelas, found the nose lined with membrane, and he is usually considered the first author to have alluded to fibrinous rhinitis. Major in 1886 fully reports a typical case in a girl aged eighteen, in whom the disease lasted three months, but it was not until 1887 that the affection seems to have attracted much attention. In that year Seifert reported three cases. One was an adult and two were children, sisters. Both the latter had also tonsillitis. There was no general disturbance, and he considered the disease distinct from diphtheria.

Moldenhauer reports four cases, and although there was diphtheria in Leipzig at the time, there was no history of direct infection in these cases, and he believes the diseases have no connection.

Also Henoch reports one and Hartmann six cases, all in children, with no spread of infection, although one case occurred in a home for deaf-mutes. In 1888 Ryerson reports a unilateral case, and Hammond one (himself) without suspecting diphtheria; and Bischofswerder three cases in which he carefully excluded all connection with diphtheria.

In 1889 Gluck and Porter in America express very similar opinions about the disease, stating that it is common and has no connection with diphtheria, but is a severe and chronic form of ordinary coryza.

In 1890 Chapin reports the case of two little children, sisters, and Raulin four cases, three in adults, one of whom

had also a patch of exudation on the pharynx. Both observers exclude all connection with diphtheria.

In 1891 Newcomb reports two cases, Leemans two, Lieven two, Hunt one; and the disease is discussed by others, as MacDonald, Hajek, &c. Up to this date over thirty-three cases have been fully recorded, some observers giving no numbers but stating that the disease is common.

In no case could any connection with diphtheria be discovered, and the disease was by all considered quite distinct. The society to whom Leemans showed his cases declared it was unnecessary to go into the differential diagnosis, no one could confound them.

In 1892 the *rôle* of the Klebs-Löffler bacillus was becoming generally recognised, and the results of the bacteriological examination of these cases were reported and changed the views of its pathology. Baginsky always found the Klebs-Löffler bacillus present, and considered the affection to be a mild form of diphtheria. Park found the bacillus in all of ten cases, in one of which the tonsil was also affected. Stamm and Abbott each found it in three cases. Other observers, however, as Abel, Van Starck, Fränkel, Sedziak, Ritter, &c., failed to obtain it. In this year also Concetti published five cases, in two of which he found the Klebs-Löffler bacillus. His cases should, however, be rather considered as true nasal diphtheria, as he himself calls them. In one of them the disease spread to the larynx, in two cases gave rise to diphtheritic infection, and in one was followed by paralysis of the palate, &c.

In more recent years numerous papers and references to the disease are found, chiefly in German and American literature. Most observers, relying on the results of bacteriological examination, consider the disease a form of diphtheria, and discuss the cause of the mildness of its symptoms.

Perhaps the most careful papers are those of Park and Abbott above alluded to, and those of Ravenel, who reports ten cases, of Gerber and Podack, who observed

six cases, and of Pluder, who also observed six cases. Some results and conclusions of these observers will be discussed later.

The following is a brief analysis of the chief clinical features presented by the thirty-six cases which I have recently observed.

1. *Sex and age.*—Twenty cases occurred in girls and sixteen in boys. Their ages varied from 10 months to 15 years. Nine cases were in children under 4 years of age, twenty-four were aged 4 to 8 years inclusive, one was 9, one 11, and one 15. This proves conclusively that the disease is essentially one of childhood, although cases occurring in adults have occasionally been reported.

2. *Season.*—The cases varied much in frequency with regard to the season of the year; thus of twenty-four cases seen in the last year, from October to March 9 were seen, in April, May, and June only 1, in July 3, in August 6, and in September 5. Thus nearly half the cases were seen in the two months August and September, and looking through my case-book I find a similar result for the previous year.

3. *Nasal obstruction* was constantly observed, the affected nostrils or nostril being completely blocked. This was usually the most prominent symptom, and the one for which relief was sought.

4. *Nasal discharge* was also constantly met with, but varied much in character and amount. In a few cases it was very slight and almost unnoticeable. In other cases a profuse, clear, watery discharge was constantly dripping from the nose. In other cases, again, the discharge was described as a thick yellow matter, or, rarely, as stained brown with blood. Towards the end of the disease "bits of flesh" were occasionally extruded from the nose. In every case in which I have examined the discharge microscopically pus corpuscles were found in it, although, as will appear later, the disease was then late in its course. The discharge was never fœtid.

5. *Bleeding* from the nose occurred in about two thirds

of the cases. In most it was slight, and occurred late in the disease, when the membrane was separating, and in many cases was probably induced by traumatism, picking at the nose, efforts at syringing, &c. In a few cases the discharge was frequently blood-stained, and in three there was epistaxis to a very serious amount. Thus bleeding is certainly not a reliable symptom for diagnostic purposes, although by some observers great stress has been laid on it.

6. *Excoriation* of the anterior nares was present in the large majority of cases, although in some it was very slight. In some impetiginous crusts appeared over the upper lip, and in three cases there were pustules on the face and hands. In no case did any membranous deposit occur on these spots, nor could any bacilli be cultivated from them.

7. *Examination of the nose* usually showed a thin, whitish, flaky, somewhat adherent exudation on the inferior turbinals, floor of nose, and septum. The nasal obstruction prevented a view of the deeper parts being obtained. The mucous membrane seemed congested, and bled easily when touched with the probe. It is a striking circumstance that in the great majority of cases the area of fibrinous exudation was absolutely limited by a sharp line corresponding with the anterior extremity of the inferior turbinal; in no case did it extend to the vestibule. In a few cases the fibrinous exudation was limited to a much smaller patch, or a loose piece only of thick membrane was found in the nose.

In eight of the cases, that is nearly one fourth, the affection was strictly unilateral. In these cases the symptoms strikingly resembled those of a foreign body in the nose, and in four of them search was made under an anæsthetic, with the result that large thick pieces of membrane were removed. This membrane resembled in all respects diphtheritic membrane, but usually seemed to be quite loose in the nose.

8. *Examination of the throat* in thirty-two of the cases

yielded a negative result, although in four of these cases there was a history obtained of sore throat at the commencement of the disease. This seemed to be very slight, and lasted but a day or two, and there was nothing apparent when the cases came under observation.

In four cases there were definite lesions in the pharynx. In one case, a boy aged 15, there was present inflammation of one tonsil much resembling follicular tonsillitis. The tonsil, however, was not much swollen nor much reddened, and the exudation from the crypts was more profuse than usual. This exudation was quite soft, creamy material, was easily wiped away, leaving a non-bleeding, slightly congested surface, and spread over the tonsil slightly on to the pillars of the fauces, and on to the lateral pharyngeal band of the same side. The throat was not tender and the glands were not enlarged.

In another case there were one or two white specks on the lateral pharyngeal bands, which were slightly inflamed.

In the other two cases these lateral bands were covered by a thin, whitish, translucent, adherent exudation which extended up to the post-nasal space. There was no swelling or inflammation of the throat, and no pain on deglutition. This condition lasted two or three weeks after coming under observation, and if the history obtained be reliable had previously existed some week or two.

These chronic cases of pseudo-membranous exudation in the pharynx and post-nasal space I have also observed quite apart from fibrinous rhinitis. The affection may last one, two, or more months, is usually confined to the lateral pharyngeal bands, is accompanied by very slight inflammation, never produces more than slight soreness, in no way affects the child's health, and is, in fact, usually discovered by some casual examination of the throat. Dr. MacDonald has described similar cases, the average duration of which was ten weeks. Some ob-

servers state that fibrinous rhinitis never follows nor is associated with a similar condition in the pharynx, but this statement, although generally correct, cannot be accepted as absolute.

9. *The general symptoms* were in every case unimportant, and this is one of the most marked features of the disease. In the majority of cases close questioning elicited the fact that the children had been somewhat indisposed at the commencement,—slight feverishness at night, headache, languor, diminished appetite, restlessness, &c., having been noticed. These symptoms passed off in a day or two, and were in no case sufficiently severe to confine the child to bed, or to make the mother seek advice. In some cases no history of initial disturbance at all could be obtained, and the children in most cases were allowed to play about or attend school as usual. Until they came under treatment, some of them did not miss a single day's attendance at school.

The insignificance of the general symptoms may also be gathered from the fact that about two thirds of the cases did not come under observation until the disease had lasted three weeks or longer, the chief symptom for which advice was then sought being the local discomfort.

Again, some cases were brought up for quite other reasons,—thus one child attended for a tubercular sinus in the neck, one for a suppurating ear, two were sent to me as probable cases of foreign body in the nose, and two children, sisters of others similarly affected, were brought up at my request to see the other members of the family. In these cases the mothers had noticed the children had a slight cold, but regarded it as of no importance.

The case of the boy aged fifteen commenced whilst he was in hospital, and I am indebted to Dr. Burney Yeo for permission to make use of it. He had bilateral fibrinous rhinitis with some exudation in the post-nasal space and on one tonsil, as above described. The temperature reached 99·8° on the first evening of the affection, but it had occasionally gone up higher than this on other occasions. After-

wards it remained normal throughout the affection, which lasted five weeks. There was no general disturbance of any kind and no sequelæ. This is the more remarkable because of the extent of the local affection, and because the patient was suffering from severe diabetes. The urine contained 2500—3000 grains of sugar per diem, albumen, and occasionally acetone. The boy weighed only 5 st. 4 lbs., and was steadily losing ground.

Even thoroughly competent observers may overlook these cases. A case I have quite recently seen was for eight weeks an in-patient in the surgical ward of a children's hospital, and was considered to have only a bad cold. I was not asked to see him until fourteen weeks from the commencement of the trouble. In another children's hospital also I have recently been informed of a case which those of the staff who saw it pronounced not to be diphtheria, whatever else it might be.

10. *Progress.*—The disease runs a subacute, occasionally almost a chronic course, the duration varying from three to twelve weeks, the average being about five weeks.

11. *Prognosis and sequelæ.*—Some of the children during the course of the disease became rather pulled down and looked pale and languid, but the large majority remained throughout in their usual health. They were kept under observation two to three months, and in none were any paralytic phenomena observed, such as loss of knee-jerk, paresis of palate, &c., although these were regularly sought for.

In every case complete recovery took place, but in two instances there were observed some adhesions between the inferior turbinate and the septum.

12. With regard to the *causation* of the disease, apart from infection, which will be discussed later, I have been unable to make out anything definite. Two of my cases followed severe blows on the nose—a fact to which I should attach slight importance, although Pluder and others have recorded similar cases, regarding the blow as a predisposing cause. Dr. MacDonald considers previous attacks

as a predisposing factor, and I have seen one typical case recurring two successive springs in a young girl. In one of the present cases a relapse occurred after a five months' interval, the first attack lasting one month, the second three months.

Diseases of the nose, such as atrophic rhinitis (of which several instances are recorded), and such affections as measles, scarlet fever, and influenza, must undoubtedly be considered predisposing causes.

True diphtheria may also undoubtedly attack the nose. The affection commences acutely, the nose is completely blocked, and membrane may be seen in it on examination. The discharge is profuse, thick, and purulent, and usually brown from admixture with blood. It is very acrid, producing much irritation of the lip, and is usually peculiarly fœtid. Epistaxis is also a common symptom, and occurs quite early in the disease quite apart from traumatism. The general symptoms are all pronounced, the child is quite prostrated and evidently extremely ill. Albuminuria is commonly seen and is often marked. The local affection is always bilateral, and it may spread to the throat as typical faucial diphtheria. The severe general symptoms continue and increase in gravity. Statistics of the North-Western Fever Hospital show that diphtheria affecting the nose is the most dangerous of all forms, the fatal cases being 67 per cent., and this is in general accord with the experience of others.

In the cases which survive, paralytic phenomena are common and severe.

This affection from its very acuteness is rarely seen in the throat departments. Two cases have, however, come under my care during the last year in which a purulent nasal discharge has persisted after an attack of diphtheria. One of these cases had suffered from faucial diphtheria and been treated in a fever hospital for some six weeks. It was brought to me about a fortnight after its return from the hospital with a purulent discharge still continuing from the nose, although no membrane could be seen, and

with paralytic symptoms, viz. weakness of the legs, loss of knee-jerks, and complete palatal paralysis. On its return from hospital one of its brothers had taken diphtheria and had died. This patient was promptly sent back into isolation.

Another case was similar, having been treated at home for a severe sore throat which confined her to bed for about a week. A month later when I saw her there was a purulent discharge from the nose, weakness of the legs, and paralysis of the soft palate. Another child in the same house, a playmate, came to me at the same time with a small membranous deposit in the throat and a discharge from the nose. At the same time the child looked pale and ill, although it was not really bad. Later it developed paralysis. In none of these cases could the diagnosis be in doubt.

Comparing fibrinous rhinitis with nasal diphtheria, we find that the latter is an acute affection characterised by very serious constitutional disturbance, that the prognosis is most grave, and that in cases which survive paralytic sequelæ are common. Fibrinous rhinitis, on the other hand, is marked by the very slight amount or complete absence of general symptoms, the entire absence of all sequelæ, the absolutely good prognosis, and the relative chronicity of the affection. The local signs in nasal diphtheria are more acute and more severe, bleeding is more frequent and occurs early quite apart from traumatism, the discharge is usually fœtid, the affection is bilateral, and may spread to the fauces as typical diphtheria. Fibrinous rhinitis is chronic, bleeding rarely occurs till late and is rarely much, being due to slight traumatism ; the discharge is rarely fœtid. The affection is freqently unilateral, and is usually limited to the nasal mucosa. When the throat is involved the appearances are characteristic, and distinct from what is usually recognised as diphtheria.

Without denying that intermediate cases may occur, clinical differences between the two affections are com-

monly so well marked that the older observers without exception did not hesitate to pronounce them distinct diseases if the possibility of their identity ever occurred to them.

Bacteriological investigation.—All the cases of this affection coming under my observation during the last fourteen months (thirty-three in number) have been examined bacteriologically, and in all very definite results have been obtained.

In many cases where the nasal discharge was easily obtainable it was examined at once by smearing it on cover-glasses, fixing, and staining with Löffler's solution of methylene blue. In the early cases numerous clumps of typical Klebs-Löffler bacilli were readily distinguished, but when weekly examinations were made the bacilli diminished rapidly in numbers as the discharge became less.

This method is of great use as a means of rapidly forming a diagnosis, and although a negative result cannot be regarded as conclusive, I have never failed to find numerous bacilli in cases where the discharge was profuse.

In every case tubes of Löffler's blood-serum were inoculated with the nasal discharge or membrane, and incubated in the hot incubator (37° C.) for eighteen to twenty-four hours. In all the cases an abundant growth of the typical Klebs-Löffler bacillus was obtained. In fifteen cases the bacillus was found in apparently pure culture, in eighteen cases there were also present staphylococci, streptococci, and occasionally other organisms.

The bacilli were nearly always (twenty-seven out of thirty-three) of the large variety, some exceptionally large, and they showed all the morphological characteristics—bipolar staining, metachromatism, polymorphism, &c.—of the true Klebs-Löffler bacillus.

In some cases cultures were inoculated every week from the nose, and the bacilli were found to persist

throughout the course of the disease, but had often disappeared in a week, and were never found a fortnight after the cessation of the discharge. They retained the same type throughout.

Recently many bacilli closely resembling the Klebs-Löffler bacillus have been described, and I have therefore carried out some experiments to establish the identity of the bacilli found in these cases.

A. The bacilli were obtained in pure culture when necessary by repeated inoculations on serum or by plate-cultures on agar. They were then sown on other media, as agar and gelatine.

In each case the growth of the colonies and the cover-glass preparations from them were similar to those of the true Klebs-Löffler bacillus. On litmus sugar-agar a distinct acid reaction was obtained.

B. *Experiments on animals.*—In twenty-three of the cases a pure culture of the bacillus was inoculated into peptone beef-broth and incubated for forty-eight hours at 37° C. If, after incubation, the culture on examination proved still pure, a portion of it was injected subcutaneously into a guinea-pig. The doses used varied. In seven cases a dose of 2 c.c. was given, which proved fatal in six instances within two days, and in the remaining instance within three days. In nine cases doses of 1·5 c.c. were given, and six guinea-pigs died within two days, two within three days, and one within four. In two other instances doses of 1 c.c. proved fatal in thirty-six hours each. In the last five cases smaller doses of 0·5 c.c. were used. One guinea-pig died in about twenty-four hours, two in forty-eight, and two in three days.

In every case post-mortem examination showed intense hæmorrhagic œdema at the site of injection, and apparently the longer the animal survived the more marked was this local reaction.

In one case a rabbit was tracheotomised and the tracheal mucous membrane rubbed with a pure culture

of the bacillus. The animal died on the third day. The whole neck and part of thorax was extremely œdematous with small scattered hæmorrhages, and there was a membranous exudation lining the whole trachea and extending down to the bronchi.

Thus the virulence of the bacilli, as tested on animals, was found to vary, but in every case was considerable, and this is a further proof of the identity of the bacillus with the true Klebs-Löffler bacillus.

In ten cases the virulence of the organisms was not tested. In eight this was due to the fact that the bacilli were not easily obtainable in pure culture. Although they appeared in many instances to be at first almost pure, other organisms grew abundantly in the sub-cultures, and the Klebs-Löffler bacilli rapidly disappeared. In some cases even by plate-cultures no bacilli could be obtained. This fact was also observed by Ravenel in some of his cases, and led him to believe that the bacilli were not very virulent, and especially were less likely to spread infection. As a rule, however, the bacilli showed their vitality when grown on blood-serum by rapidly crowding out other organisms, pure cultures being readily obtainable simply by the process of making repeated sub-cultures. I kept some of my cultures alive over seven months, transferring them to fresh tubes not oftener than once a month or six weeks.

Nearly all the failures occurred during last summer, when I was unable to give daily attention to the work, and I attribute the fact not so much to the feeble vitality of the Klebs-Löffler bacillus as to the increased growth of the associated organisms, sarcinæ, &c., while the cultures were laid aside. In no case did a pure culture die out if re-inoculated about every four weeks.

c. *Toxin-producing experiments.*—Dr. Macfadyen suggested that I should test the toxin-producing powers of the bacilli. For this purpose pure cultures obtained from typical cases, No. 1 of bilateral and No. 2 of unilateral fibrinous rhinitis, were taken, together with a third culture,

No. 3, obtained from a case of severe faucial diphtheria to act as a control.

Flasks containing about 70 c.c. of peptone beef-broth were inoculated from these cultures and grown for sixteen days. These cultures were then examined, and no foreign organisms being discovered they were sterilised by filtration. To the clear filtrate ½ per cent. carbolic acid was added. The toxins being thus obtained, the following experiments were made. A dose of 0·5 c.c. of toxin No. 1 (prepared from the bilateral fibrinous rhinitis case) killed a large guinea-pig in thirty-six hours, a dose of 0·1 c.c. of the same toxin being fatal in the same time. The latter result was so unexpected and indicated such a powerful toxin that the experiment was repeated on three occasions, always with a like result.

Doses of 0·5 c.c. and 0·1 c.c. of toxin No. 2 prepared from the case of unilateral fibrinous rhinitis were fatal in thirty-six hours and four and a half days respectively. Similar doses of the No. 3 toxin (the diphtheritic one) killed in three and a half and four and a half days respectively. Doses of 1 c.c. of No. 2 and No. 3 were also given, and both proved fatal in thirty-six hours. Thus one of the toxins obtained was at least equally virulent, and one much more so, than that obtained from the diphtheria bacilli which was used as a control.

D. *Experiments with antitoxin.*—Experiments were next performed to determine if these toxins were neutralised by the diphtheria antitoxin as sold for remedial purposes. Of toxin No. 1 doses of 0·5 c.c. were injected into two guinea-pigs, together with 1 c.c. and 0·5 c.c. of antitoxin. The animals lived for six and eighteen days respectively. Further, a dose of 2·5 c.c. of this toxin, that is twenty-five times the dose shown to be fatal in thirty-six hours, was injected into a guinea-pig with 0·25 c.c. of antitoxin, and the animal lived for thirteen days. Of toxin No. 2 doses of 1 c.c. and 0·5 c.c. were injected with similar doses of antitoxin: the animals lived nine days. With a dose of 0·1 c.c. of toxin and 0·1 c.c. of antitoxin

the animal survived. Toxin No. 3 (the control) was used in doses similar to No. 2, and the animals survived eleven days.

Although these experiments are not entirely satisfactory they conclusively prove the neutralising effects of the diphtheria antitoxin on the toxins obtained from the bacilli of fibrinous rhinitis. The death of the animals in some of the cases is probably due to the fact that such large doses of toxin were given, the antitoxin acting as a certain antidote only when the minimum fatal doses of toxin are used.

Similar results were obtained when antitoxin was injected together with living cultures of bacilli. Thus in one case 0·5 c.c. of forty-eight hours' broth culture was fatal in twenty-four hours. Given with 0·5 c.c. antitoxin the animal survived six days. In another case the same dose of broth culture killed in three days; given with antitoxin the animal survived. In a third case 0·5 c.c. of broth culture killed in three days; given with antitoxin the animal survived.

The results of these experiments, briefly stated, show that in cases of fibrinous rhinitis an organism is constantly found in extraordinarily large numbers which resembles, morphologically and by its growth on various culture media, the true Klebs-Löffler bacillus. The bacillus is of varying but usually great virulence, is capable of producing virulent toxins, and these toxins as well as cultures of the living bacilli are neutralised by diphtheria antitoxin. The bacilli inoculated on the mucous membrane of a rabbit's trachea produced an extensive membranous exudation, resembling that of human diphtheria.

These experiments place beyond doubt the identity of the bacilli with the true Klebs-Löffler bacillus, and also show that the mildness of the affection in no way depends upon the slight virulence or feeble toxin-producing powers of the organisms.

Thus, as to the identity or non-identity of fibrinous

rhinitis with diphtheria, the bacteriological evidence is in direct opposition to the clinical. Further evidence of the greatest importance can be obtained by a careful clinical and bacteriological examination into the surroundings of these cases, and of the persons with whom they come in contact. The great facilities this affection offers for a wide-spread diffusion of infection is apparent when we consider that the nasal discharge in most of the cases was profuse, and was constantly dripping from the nose or being sneezed about over everything; that it was swarming with bacilli, that it lasted as a rule several weeks, and that owing to the absence of general symptoms the children were not seen medically until two or three weeks from the commencement of the disease. For the same reason the affected children attended school, and played with other children as usual. Belonging to the poorer classes, a whole family with many children often lived in one room, necessarily in close contact, and to further aid the spread of infection the mother would use her own handkerchief to the noses of all the children.

This inquiry into the patient's surroundings falls naturally into three headings.

1. Could these cases of fibrinous rhinitis be directly traced to diphtheritic infection?

2. Was there found a wide-spread diffusion of the bacilli as is above presumed? and—

3. Did outbreaks of true diphtheria arise in connection with these cases?

In regard to the first point I could only find one case in which diphtheria might have been the cause of infection, and this is somewhat doubtful. The patient's father was said to be suffering from diphtheria, but the patient, a child aged 1 year and 10 months, was, at the time I saw it, and had been for three weeks previously, living with another family, and had not been in any communication with its father. I cannot determine if the father really had true diphtheria or such

a sore throat as I shall later describe, but the child showed no sign of it, nor did it occur amongst the other children (five) with whom this patient was living. Of course diphtheria was all the time very prevalent in London, but my cases did not correspond in frequency with the reported cases of diphtheria (the numbers of course are very small); nor was there any special incidence of diphtheria in the schools these children attended.

In three cases, and in a fourth which I have lately seen, there was a definite connection with scarlet fever. These cases and the case of diphtheria above mentioned may quite well have been mere coincidences.

These results are confirmed by nearly all other writers, including the whole of the older observers; and amongst the more recent ones, Ravenel in ten cases, Gerber and Podack in six cases, Park and Abbott six and three cases, although all these latter believe firmly in the diphtheritic nature of fibrinous rhinitis. Pluder in six cases found one in which there had been diphtheria six weeks previously in the house then occupied by another family. Johannessen reports one case in connection with an outbreak of diphtheria in a children's hospital, and there are a few others reported without any details by Eeman, Hunt, &c. Most observers state that they have especially endeavoured to obtain evidence of such infection, and have been able to exclude it. It may, I think, be concluded that diphtheria very rarely gives rise by direct infection to fibrinous rhinitis. With regard to the second and third points I obtained such striking results that some of the cases must be dealt with individually.

Cases 1, 2, and 3 occurred in the persons of three children in one family, two girls and a boy. The boy, aged 6, was first attacked, and a week later his two sisters, aged 4 and 9 years, were attacked. All three patients suffered in exactly the same way with typical bilateral fibrinous rhinitis which lasted six to eight

weeks. About five weeks from the commencement of the affection the mother had a sore throat, which lasted two to three days, and was not at all severe. She was not laid up with it, and had no subsequent ill effects. The other people in the house, a father and a two-year-old daughter, remained well throughout.

There was no history of diphtheria in connection with these cases either before or after. It was not prevalent in the district, and there had been no case at the school the children attended.

Cases 10 and 11.—A girl aged 4½ was brought to me with a small sinus in the neck. She was noticed to have a discharge from the nose, and on inquiring the mother informed me she had noticed the child had a cold in the head for the last three weeks. It was seen to be a typical case of bilateral fibrinous rhinitis with complete absence of general symptoms. Virulent Klebs-Löffler bacilli were found both in the nose and in the pus from the sinus. The child's sister was said also to have a slight cold, and being brought to me was found to be similarly affected. Three adults in the house remained well.

Cases 28 and 29.—Two sisters, aged 6 years and 13 months, with bilateral fibrinous rhinitis. The elder child was affected a month before the younger, and had attended school throughout, only coming under observation about the fifth week of the disease. The father, mother, and another sister, aged 2½, living with them, remained well. Three other families with nine children living in the house, and all remained well.

Cases 32 and 33.—A girl aged 5½ was sent to me as a case of foreign body in the nose, unilateral nasal discharge having been present about fourteen days. Under chloroform a large thick piece of membrane was removed from the affected nostril. A week later the child's sister, aged

ten months, was brought to me similarly affected with unilateral fibrinous rhinitis. The other people in the house, all adults, remained well.

Thus out of my thirty-six cases nine occurred in four families. In three other instances other children in contact with these cases were said to have sore noses or colds in the head, but I did not see any of them.

In connection with the above group of cases it was noted that in one instance the mother of the child had a sore throat. Other instances are as follows :

Case 9, a boy aged 15, in King's College Hospital, under the care of Dr. Burney Yeo, who was treating him for severe diabetes as above described. Through the courtesy of the staff I was able fully to investigate the surroundings of this case. All the patients who had been some days in the ward and the nurses were examined, and cultures made from the tonsils. They numbered in all thirty-two. Of these twenty-one showed no bacilli on cultivation, and suffered from no throat affection. Of the remaining eleven, two showed numerous colonies of the pseudo-diphtheria bacillus of Von Hofman in pure culture, and without any symptoms of sore throat. The remaining nine gave cultures of typical Klebs-Löffler bacilli. These cases are briefly as follows :

i. Boy aged 12, under treatment for pericarditis, but now allowed to get up. He had no sign or symptom of sore throat. Cultures showed numerous colonies of pure Klebs-Löffler bacilli.

ii. Man aged 45, allowed to be up in ward. Had no sign of throat trouble. Numerous colonies of Klebs-Löffler bacilli.

iii. Adult. Had had no sore throat. One colony of Klebs-Löffler bacilli obtained.

iv. Nurse, who said her throat was not and had not been sore, but the tonsils appeared slightly red and enlarged. She remained constantly on duty. Numerous

colonies of Klebs-Löffler bacilli obtained in pure culture. Six weeks later this nurse had a sore throat, but no bacilli could then be found.

v. Boy, under treatment for pericarditis, says throat has not been sore, and there is nothing to see on examination, but the glands at the angle of the jaw have been slightly enlarged and tender the last two days. Numerous colonies of pure Klebs-Löffler bacilli obtained.

vi. Boy had a slight sore throat lasting two days only, with swelling and redness of the tonsils. Fairly numerous colonies of Klebs-Löffler bacilli, with other organisms, obtained on cultivation taken two days after the sore throat had got well.

vii. Boy aged 18, suffering from advanced diabetes. White patches of exudation seen spreading over both tonsils, and glands at angle of jaw enlarged. Temperature reached 101° F. once only on the first day. There was no general disturbance and no sequelæ. He was quite well by the fourth day.

viii and ix. Two nurses with rather severe sore throats and some general disturbance at first. Clinically follicular tonsillitis with somewhat profuse exudation. Numerous colonies of Klebs-Löffler bacilli obtained in each case. The general disturbance subsided in a few days, and there was no subsequent trouble.

Thus we have here among thirty-two people exposed to infection from one case of fibrinous rhinitis, twenty-one free from any sign of sore throat or bacilli, at least on the one occasion on which they were examined; two in whom pseudo-diphtheria bacilli were found without any throat trouble; three in whom Klebs-Löffler bacilli were found, in two of which they were numerous, and all three without throat trouble; and six cases in which more or less sore throat occurred in conjunction with numerous bacilli, generally in pure culture. One case of sore throat of a similar kind had occurred just before in the ward, but had not been examined bacteriologically. Excluding

this one we have six cases of sore throat and one case of fibrinous rhinitis *plus* sore throat, all arising in association with each other, some of the patients being already in a very depressed general condition, and yet none of them presented any feature clinically characteristic of diphtheria.

The results obtained in this case I have quoted fully, as I was able to make such a complete inquiry; but they are confirmed by those obtained in other cases, some of which are briefly as follows:

Case 7.—Boy aged 7½, suffering from bilateral fibrinous rhinitis and the typical form of pharyngeal affection which has been above described as sometimes associated with this disease. The affection lasted ten weeks. The mother and three children lived with this boy, and all remained well but one sister. The latter, aged 12, had a sore throat lasting two days, which was not severe enough to prevent her attending school. She was brought to the hospital four days after the attack at my request. Nothing abnormal could then be detected in the throat, but typical Klebs-Löffler bacilli were obtained from the tonsils by cultivation on serum. They formed numerous colonies in almost pure culture, and proved to be of full virulence, 1·5 c.c. of forty-eight hours' broth culture killing a guinea-pig in forty-eight hours.

Case 8.—Boy aged 5, with bilateral fibrinous rhinitis, lived with his father, mother, and two other children. The father and one child remained well throughout, and no bacilli were obtained from their throats. The mother had a sore throat about the time the boy was first attacked. I did not see her, but as far as I could ascertain it was only slight, and caused her no subsequent trouble. The other child, aged 2½, had a similar sore throat at the same time, which lasted two to three days. When I saw the family three weeks later this child appeared quite well and the throat was normal, but

cultivations from the tonsils yielded a numerous growth of true Klebs-Löffler bacilli. Four other people in another flat of the same large dwelling-house were said to have had sore throats which were not diphtheritic, and did not seriously indispose them. I saw none of them.

Case 12.—Boy aged 5, with unilateral fibrinous rhinitis lasting one month, and recurring again in five months and lasting three months. He lived with his father, mother, and two brothers, and one of the last had a slight sore throat two months before being seen. Cultivations from the mother's throat showed no bacilli; from the two brothers the pseudo-diphtheria bacillus was obtained.

Case 13.—Boy aged 3, with unilateral fibrinous rhinitis, came under observation on the fourteenth day of the disease. The mother and one sister had had sore throats, the other sister remained well. No bacilli were obtained from any of them.

Case 15.—Boy aged 4, a rather severe unilateral case. Of the father, mother, and three other children one only of the last had a slight sore throat. Cultivations made from the throat showed pure cultures of Klebs-Löffler bacilli in the case of the mother and one sister, and yielded negative results in the other cases.

Case 16.—Girl aged 7, with bilateral fibrinous rhinitis with much discharge, was seen on the fourteenth day of the disease. The child's mother and sister had slight sore throats a week before the child was seen, and the only other person in the house, a man aged 19, had a slight sore throat a week later.

Case 19.—Girl aged 6, a slight unilateral case, lived with her mother and two sisters. All remained well, but typical large Klebs-Löffler bacilli were obtained from the throat of one child.

Case 17.—Boy aged 2, whose disease had lasted six weeks; the mother had had a slight sore throat, and the sister had had a little running at the nose. The father and three other families in the same house all remained well.

Case 20.—Girl aged 4, first seen on eighteenth day. The mother and one sister had had slight sore throats, and the baby was brought to me with slight tonsillitis. The father of the child and two other families containing nine children living in the same house all remained well.

In other instances complete absence of infection was noted. Thus Case 4, a child aged 3, came under observation in the third week, and the affection lasted three weeks longer. The discharge from the nose was profuse. The child lived in one room with the mother and four other children, all of whom were said to be quite well throughout. There were other similar cases, but it is possible that, when the family were not seen by me, mild cases of sore throat were overlooked.

Another case which I have quite recently seen is remarkable.

A boy aged 5½, who had been affected apparently about two months, was admitted to the children's hospital with impetigo on the face and corneal ulcers. These latter were treated and the nose was syringed. He was in hospital eighteen days, then in convalescent home eleven days, and then again in hospital five weeks. The disease lasted all this time, and being unrecognised no precautions as to isolation were adopted. During this time over thirty children came into more or less direct contact with him, and yet there was no case of diphtheria or sore throat in the ward apart from two cases of scarlet fever. These latter led to the closing of the ward. I did not see the boy till the end of his stay in hospital about the fourth month of the disease, when I found typical bilateral fibrinous rhinitis, and obtained by

culture a pure growth of Klebs-Löffler bacilli of full virulence. In this case the disease lasted over four months, and for nearly a month he attended school, a month he was at home and with two other families, and two months he was in hospital. Nowhere was there another case of sore throat.

Summing up these results, we find that twenty-five cases of sore throat occurred in direct connection with eleven families affected with fibrinous rhinitis. Many of these were seen by me, and presented none of the clinical symptoms of diphtheria, although from all of them the diphtheria bacillus was isolated. The other cases were all slight, and as far as the history obtained goes were not diphtheria. Also in four instances a case of fibrinous rhinitis was the apparent starting-point of the same affection in others, in one family there being three cases of it. Finally, the diphtheria bacillus was frequently found in the throats of healthy people in contact with these cases.

From these results we may conclude that fibrinous rhinitis is an infectious disease, and that it has a special tendency to reproduce itself. This fact has been expressly noted by Ravenel, two of whose ten cases were in sisters. Seifert, Chapin, and Abbott have recorded similar instances. Other observers have more or less incidentally mentioned that sore throats occurred in connection with these cases, and Pluder has especially dwelt on this point as proving the diphtheritic nature of the disease. He records six cases, in three of which spread of infection occurred.

(i) Boy aged three, with bilateral fibrinous rhinitis and small patch on one tonsil. Had four sisters exposed to infection ; two had bilateral exudation on the tonsils, and one had angina without exudation. It is noted that in all cases general disturbance was absent. All showed virulent bacilli.

(ii) Boy aged five. Had typical bilateral fibrinous rhinitis, and another two days later had hemp-seed sized

patch on one tonsil. Cultures from nose and throat showed virulent bacilli. There was a history of diphtheria in the house six weeks before this family entered it.

(iii) Young housemaid with mild naso-pharyngeal diphtheria. Next day young child in house had bilateral fibrinous rhinitis and faucial congestion. Both showed virulent bacilli, as also did cultures from throats of three healthy people in house.

In other cases the bacilli were found in the throats and noses of exposed persons, but without any morbid lesion.

Pluder considers all the above throat infections as diphtheria, but it seems to me that clinically they were distinct, and would not have been considered diphtheritic but for the bacteriological examination.

The results of other observers in the main agree with the above, and, taken all together, go far to show that fibrinous rhinitis, although it is very infectious and gives rise to throat affections, has slight if any tendency to give rise to diphtheria. Ravenel was unable to record such a result in his ten cases, although he states that he particularly sought for it; in fact, the only recorded cases I have found are those of Concetti, Gerber and Podack, Hunt, and Eeman.

Concetti describes his case as primary nasal diphtheria, and this is a more correct description of it than fibrinous rhinitis would be, for it differed from the latter in essential particulars, and was followed by paralysis. Similar remarks apply to the case recorded by Gerber and Podack. Hunt and Eeman simply relate cases without detail.

I have gone very fully into this point, as it seemed to me of the greatest importance. The affection seemed to offer such exceptional facilities for the spread of infection—and this spread of infection does indeed take place—that it seems very remarkable, if the disease is diphtheritic, that cases of unmistakable diphtheria should not occur in connection with it. And yet in thirty-six carefully observed cases I have been unable to find a

single instance of such occurrence, and the few recorded instances seem doubtful. Without, therefore, denying its possibility, its occurrence must be admitted to be extremely rare and at present not authenticated.

To obtain some information as to the diffusion of the bacillus of diphtheria, and to control my results, I made cultivation experiments from the noses of a hundred different individuals. This experiment lasted from September 29th to October 10th, and included every case of a child attending my out-patient practice and twenty-five cases from Dr. Sutherland's medical clinique. All the patients were under twelve years of age, and many were infants. There was no history in any of them of exposure to diphtheritic infection. The children were attending for a large variety of complaints, but of those in my own practice (seventy-five) more than half were cases of adenoids, and in other respects enjoyed good health. None of the patients were seriously ill. A few of the cases (four) had atrophic rhinitis, and many of them had a slight running at the nose.

The cultures were made in the usual way. Small sterilised swabs of wool on wire were inserted into the nostril and then rubbed over the surface of Löffler's blood-serum. This was incubated for eighteen to twenty-four hours at 37° C., and then examined by cover-glass preparations. In nearly every case a numerous growth was obtained. The results as regards the diphtheria bacillus were as follows :—In five cases a pure culture of the Klebs-Löffler bacillus was obtained, and in eight other cases this organism was found together with cocci, sarcinæ, &c. In sixteen cases a bacillus resembling more or less closely the diphtheria bacillus was obtained in pure culture, and in thirty-six other cases in more or less mixed growth. Further experiments have proved this bacillus to be the pseudo-diphtheria bacillus of Hofman.

Thus we find that in cultivations from the nose in children the Klebs-Löffler bacillus is found in about 13 per cent., and Hofman's bacillus in 52 per cent.

Johannessen examined the throats of twenty healthy children in the ward of a hospital in which a case of diphtheria had occurred. He found virulent diphtheria bacilli present in three cases. Later, another case of diphtheria having occurred, he found the bacilli present in four out of eighteen healthy throats.

Aaser in similar circumstances, an outbreak of diphtheria in a soldiers' barracks, found the Klebs-Löffler bacilli in seventeen out of eighty-nine healthy throats, that is 19 per cent. In an outbreak amongst some children, bacilli were found in 20 per cent. Maude reports finding bacilli in eighty-nine out of 214 healthy people exposed to infection, that is in 41 per cent. Maude also reports that diphtheria bacilli were present in forty out of 148 cases of angina said not to be diphtheritic, that is in 27 per cent. Müller finds the Klebs-Löffler bacilli present in twenty-seven cases out of 100 healthy children with normal throats—curiously the exact proportion in which Maude found them present in cases of non-diphtheritic angina. Thomas found the diphtheria bacillus (usually non-virulent) in nasal discharge in eighty out of 326 cases examined, that is 24 per cent.; and Vassant found them in similar circumstances in twenty-six cases out of 100 examinations.

These investigations show conclusively that the Klebs-Löffler bacillus is found commonly in the normal throats of healthy people who have not been exposed to diphtheritic infection, although not quite so commonly as in those who have been exposed to it; that the bacillus is found just as frequently in cases with normal throats as in cases with non-diphtheritic angina; that the bacillus commonly occurs in the healthy nose, and is found in about 25 per cent. of all cases with any form of nasal discharge.

Conclusions.—It has been claimed that just as the tubercle bacillus when found in any morbid condition is the decisive test of the tubercular nature of the affection,

so every morbid condition in which the Klebs-Löffler bacillus is found must be pronounced to be diphtheria whatever the clinical appearances. Without agreeing with this dictum it must, I think, be allowed that if the Klebs-Löffler bacillus is *constantly* found in an affection clinically characterised by the formation of membrane this affection is a form of diphtheria. Fibrinous rhinitis, however, presents in its clinical aspects and associations such marked differences from diphtheria that I think the distinction is worth maintaining. As Osler puts it, the Klebs-Löffler bacillus gives rise to two distinct affections in the nose, and I think it might be added in the pharynx also. And we adopt a similar course with regard to tubercular affections. Thus lupus of the larynx is clinically entirely distinct from laryngeal phthisis, and yet both are indisputably tubercular.

Similarly, if we admit with the large majority of recent observers that the *Streptococcus erysipelatis* of Fehleisen is identical with the *Streptococcus pyogenes*, we must still admit that erysipelas, cellulitis, and an acute abscess are distinct clinical affections, although all due to the invasion of the tissues by the same organism.

With regard to the latter organism, we know that Fehleisen, inoculating pure cultures of it obtained from a case of erysipelas into human beings, produced always erysipelas, and not other affections; and also conversely that inoculations into the skin of streptococci from an abscess, either experimentally or when an acute abscess containing them is opened, never produce erysipelas.

For these reasons Watson Cheyne among others has maintained that the organisms are distinct, and my own observations on fibrinous rhinitis, and more especially on the diseases to which it gives rise, which are really a natural series of experiments on human beings, might be used as an argument against the specificity of the Klebs-Löffler bacillus. Hanseman and others have indeed argued thus simply from the clinical differences between fibrinous rhinitis and diphtheria, and from the wide-spread

distribution of the bacilli in healthy throats. The arguments in favour of the Klebs-Löffler bacillus are, however, so overwhelming that it seems unnecessary to pursue this line of argument, and more profitable to attempt some explanation of the fact that it does give rise to two distinct affections.

1. The most obvious explanation would be that the individuals attacked are more or less immune to diphtheria. It might be urged that a local lesion is necessary to enable the bacilli to obtain a footing, that the nose is an unfavorable site for them, or that absorption of bacillary products takes place very slowly from the nasal mucous membrane, or that there is constitutional immunity in these cases. It has been urged that the absorption of toxins takes place slowly in this affection, and allows neutralising antitoxins to form in the blood sufficiently rapidly to prevent much constitutional disturbance. The absence of a local lesion may account for the fact that the bacilli are frequently found in the throat or nose without apparently producing any symptoms, but it cannot be the explanation of the absence of general symptoms, &c., when the bacilli have obtained sufficient foothold to produce a membranous exudation. Again, there seems no sufficient reason for supposing that absorption from the nose is slow or slight, but even granting this, in some of my cases the disease attacked the pharynx, and it spread to the pharynx in others, and we know that absorption takes place readily enough in this region. It is true that the affection of the throat was of a peculiarly superficial, pseudo-membranous character, but a satisfactory explanation must account for this fact. Most important of all, the affection, although giving rise to wide-spread infection did not give rise to true diphtheria, and we can hardly suppose that all the persons exposed to infection were more or less immune. They included, as we have seen, many feeble individuals in the ward of a general hospital, the surgical ward of a children's hospital, a convalescent home for children, and many large and young families.

The above theories failing, we must seek an explanation in some modification of the infecting organism or organisms. Many observers have said that the bacilli found are of feeble virulence, that they do not *kill* guinea-pigs (Abbott), or that cultures of them die out even when sub-cultures are frequently made (Park and Ravenel). Later observations and my own prove that, although the virulence of the organisms varies somewhat, in the great majority of cases it is well marked or even extreme. Further, I have shown that cultures of the bacilli can be kept alive many months even when sub-cultures were made at intervals of five to six weeks.

I have also shown that the absence of general symptoms is not due to the deficient toxin-producing powers of the bacilli, and therefore must be due to the non-absorption of the toxins formed. This latter may be, and probably is, due to the fact that the local changes, the necrosis of the tissues, is less deep in fibrinous rhinitis than in diphtheria.

Other organisms, and especially the pyogenic streptococci and staphylococci, have been considered active associates with the Klebs-Löffler bacillus in the production of severe diphtheria, and their absence to account for the mildness of fibrinous rhinitis. But these organisms are frequently found in fibrinous rhinitis, and also in the milder as well as in the severer forms of diphtheria. These pyogenic organisms, however, vary much in virulence, and can hardly be supposed to play no part in the disease. It seems possible that in diphtheria some organism is present which is not found in fibrinous rhinitis; that the latter is a simple Klebs-Löffler bacillus, and the former a mixed infection. Or, what comes to much the same thing, the organisms associated with the Klebs-Löffler bacillus, possibly the pyogenic cocci, are much more virulent in the one case than in the other. If this explanation be not the true one, the alternative seems to be that the Klebs-Löffler bacillus found in fibrinous rhinitis is not of full virulence,—that is, that the animal

experiments detailed above do not give reliable results when applied to man. Although this may be possible, one would hardly expect it, and the foregoing explanation seems to me the more likely one. But the question must remain undecided at present.

I have not touched on the treatment of fibrinous rhinitis, but the question of isolation must be considered. Nearly all observers have insisted on the absolute necessity of rigid isolation, but it is difficult to see how this can be effectually carried out. As I have shown, the patients are well enough to attend school throughout the disease, and as a rule come under observation very late in its course. Probably many other cases are not seen by a medical man at all, or if seen not recognised. Of course after they have been seen they should, in the present state of our knowledge, be isolated. Fortunately, however, the neglect of this precaution does not seem to be very harmful.

Constantly in the course of this investigation the question of the diagnostic importance of the presence of the Klebs-Löffler bacillus has arisen. The bacillus is found not only in healthy noses, but commonly in noses in association with a slight discharge. These cases surely cannot be regarded as diphtheria. If, however, they must be so considered, and means of isolation adopted, it is quite obvious nothing but a systematic and frequent bacteriological examination of the nose of every child would suffice for the detection of the cases. Neither do I think that every case of sore throat and bacilli is necessarily diphtheria. In many cases I have seen, the soreness of the throat has lasted but a day or two, with no general symptoms; in other cases there has been a slight redness; in some all soreness has been denied. In other cases there has been slight exudation, white points varying in size from a pin's head to a hemp-seed, without any inflammatory signs. Such cases would have passed unnoticed except by systematic bacteriological examination, and if they are diphtheria it seems to me that every case

in which the bacilli are found in the throat must be so considered. For it is probable that the bacilli if found in any quantity in a throat are living and multiplying there, and what degree of change must we consider morbid? Even if the throat seems perfectly normal we cannot be quite positive, or assert that it was normal the day before.

Further, having regard to the wide-spread diffusion of the Klebs-Löffler bacillus in healthy throats, it is only to be expected that we should sometimes find it in cases of sore throat having nothing to do with diphtheria, and in two whole series of cases by different observers, in different continents, the percentage of cases in which the bacillus was found was curiously enough exactly identical, viz. 27 per cent., one observer dealing entirely with healthy throats, the other with clinically non-diphtheritic angina

It seems to me that, in the present state of our knowledge, we are not justified in concluding that cases of mild sore throat without general symptoms, or any definite clinical sign of diphtheria, are diphtheria, even if the specific bacillus be present, unless they occur in direct connection with other cases of true diphtheria.

The bacteriological work was carried out at the British Institute of Preventive Medicine, where all the various culture media, animals, &c., were provided, and every facility for working was given me. For this and for much advice I have to thank the director, Dr. Macfadyen. I have also to acknowledge my great indebtedness to Dr. R. T. Hewlett, assistant bacteriologist to the Institute, who has freely given me much time and the benefit of his great experience. He has constantly assisted and advised me in every stage of my work, and has performed many of the experiments for me.

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No.	Name.	Age and sex.	Date.	Previous duration of symptoms.	Character of discharge.	Part affected.	Thr
1	S. S.	M., 6	Aug., 1896	14 days	Purulent, rather profusc	Bilateral; whole nasal mucosa	N affec
2	L. S.	F., 4	„	7 days	Do.	Do.	D
3	M. S.	F., 9	„	14 days	Do.	Do.	D
4	E. H.	F., 3	Sept., 1896	21 days	Thick, "mattery"	Large piece of membrane in *one* side	D
5	F. B.	M., 3	„	14 days	Profuse, clear	Large piece of membrane *one* side only	D
6	A. F.	F., 5	Oct., 1896	21 days	Thick, "mattery"	Bilateral; whole mucosa	? Sligh at beg
7	T. R.	M., 7½	„	8 days	Much, clear	Do.	Had litis l 14 d
8	A. B.	M., 5	Nov., 1896	21 days	Do.	Do.	Not a
9	G. E.	M., 15	Dec., 1896	2 days	Do.	Do.	Exuda tonsi desc
10	R. C.	F., 4½	Jan., 1897	14 days	Very little, mucous	Bilateral, but only shreddy patches	Not a
11	J. C.	F., 2½	Feb., 1897	10 days	Do.	Do.	I
12	G. T.	M., 5	„	?12 wks.	Do.	Unilateral patch of membrane	I
13	W. N.	M., 3	Mar., 1897	14 days	Do.	Unilateral	I
14	A. R.	M., 8	„	21 days	Purulent	Bilateral, whole nasal mucosa	I
15	V. L.	M., 4	June, 1897	4 days	Do.	Unilateral	I
16	G. R.	F., 7	July, 1897	14 days	Do.	Bilateral, whole nasal mucosa	Not

[1] Dose of 48-hour culture

General symptoms.	Duration.	Organisms found.	Virulence of the K.-L. bacilli.[1]	Family surroundings of patient.
·ht head-, languid, &c.	6 weeks	No cultures	—	One family. The mother had a slight sore throat; father and 1 other sister remained well. Scarlet fever at the school.
Do.	4 weeks	Do.	—	
Do.	8 weeks	Do.	—	
guid and ritable	6 weeks	Pure large K.-L.	1·5 c.c. in 36 hours	Mother and 4 children remained well.
·y slight	5 weeks	Do.	2·0 c.c. in 36 hours	Father and mother remained well.
dache for day, but ded school through	6 weeks	Do.	1·5 c.c. in 36 hours	Mother and 1 brother remained well (source of toxin No. 1).
really ill, general inposition; , &c., all hrough	10 weeks	Large K.-L. and streptococci	1·5 c.c. in 2 days	One sister aged 12 had sore throat for one day and virulent K.-L. found a week later; mother and 1 sister remained well.
ight at ming only	6 weeks	Large K.-L. and few coeci	1·0 c.c. in 2 days	Six people in house had slight sore throats.
ry slight	5 weeks	Do.	Do.	Thirty-two people exposed. 21 normal, 6 had sore throats and K.-L., 3 K.-L. only, and 2 pseudo-diphtheria bacilli only.
None	3 weeks	Large K.-L. pure	1·5 c.c. in 2 days	Patients are sisters. 3 adults in house were well (K.-L. also found in sinus in neck of R.C.)
Do.	3 weeks	Short K.-L. pure	1·5 c.c. in 4 days	
Do.	14 weeks	Do.	1·5 c.c. in 3 days	Two adults well; 2 brothers had pseudo-bacilli, 1 had a sore throat. Similar attack 5 months ago.
Do.	3 weeks	Large K.-L. mixed	1·5 c.c. in 2 days	Mother and 1 sister sore throat. 1 sister well.
r and light position at first	10 weeks	Do.	1·5 c.c. in 3 days	Two adults remained well.
Slight riousness" at first	4 weeks	Do	Not tested; bacilli died out	Father, sister, and brother well; mother and sister had K.-L. only; 1 brother had sore throat.
ht at first	6 weeks	Large K.-L. mixed	1·5 c.c. in 2 days	Two adults and 1 sister had sore throats.

[1] required to kill a guinea-pig.

No.	Name.	Age and sex.	Date.	Previous duration of symptoms.	Character of discharge.	Part affected.	Throa
17	N. V.	M., 2	July, 1897	6 weeks	Thick, slight	Bilateral in patches	Slight at
18	L. T.	F., 2½	„	14 days	Much, clear	Do.	Not affe
19	L. A.	F., 6	Aug., 1897	9 days	Thick, slight	Right side only, patch	Slight at
20	L. U.	F., 4	„	18 days	Purulent	Bilateral	Slight pa tonsilli
21	G. W.	M., 11	„	? 6 weeks	Crusty and thick	Bilateral patches	Not affe
22	A. P.	F., 8	„	14 days	Much, clear	Bilateral and all nose	Do.
23	H. E.	M., 6	Sept., 1897	?	Do.	Do.	Do.
24	E. C.	F., 5	„	7 days	Do.	Bilateral shreddy patches	Redne
25	F. A.	F., 6	„	10 days	Do.	Do.	Not affe
26	M. P.	F., 7	„	14 days	Do.	Bilateral and all nose	Do.
27	L. B.	M., 8	„	21 days	Do.	Do.	Do.
28	E. G.	F., $1\frac{1}{12}$	Aug., 1897	5 weeks	Thick, slight	Do.	Do.
29	L. G.	F., 6	„	1 week	Do.	Do.	Do.
30	D. S.	F., 3½	Oct., 1897	4 weeks	Thick and bloodstained	Do.	Do.
31	H. M.	M., 5	„	3 weeks	Much, thick	Do.	Do.
32	L. E.	F., 5½	„	2 weeks	Thick, slight	Unilateral	Do.
33	D. E.	F., $1\frac{10}{12}$	„	7 days	Clear, slight	Do.	Do.
34	F. L.	M., 6	„	14 days	Clear at first, later thick	Bilateral	Slight 2 day
35	H. S.	M., 4	„	14 days	Do.	Do.	Non
36	L. W.	F., 4	„	7 days	Do.	Do.	Non

General symptoms.	Duration.	Organisms found.	Virulence of the K.-L. bacilli.	Family surroundings of patient.
nor, pallor, &c.	12 weeks	Pure short K.-L.	2·0 c.c. in 2 days	Father well; mother sore throat; sister sore nose. Three other families in house remained well.
None	4 weeks	Short K.-L. mixed	Died out	All well.
None	3 weeks	Large K.-L. mixed	2·0 c.c. in 2 days	Mother and one sister = well; one sister = K.-L.
nd languid	5 weeks	Large K.-L. pure	Do.	Father = well; mother and sister = sore throats. Two families with nine children = well.
nt debility	18 weeks	K.-L. and cocci	Died out	All well.
ish at first	7 weeks	Do.	Do.	Two adults and five children = well.
None	+ 4 wks.	Pure large K.-L.	2·0 c.c. in 3 days	All well.
ry slight	3 weeks	Do.	2·0 c.c. in 2 days	All well.
Slight	5 weeks	Large K.-L. mixed	Died out	All well.
Do.	5 weeks	Large K.-L. pure?	Do.	All well.
eadache, llor, and eakness	4 weeks	Large K.-L. mixed	2·0 c.c. in 2 days	Father, mother, and two children = well.
; at school through	7 weeks	Short K.-L. mixed	Not tested	Sisters. One other sister, father, and mother = well. Two other families, all well.
None	3 weeks	Do.	Not tested	
Slight	6 weeks	Large K.-L. mixed	Died out	Another child sore nose.
chool all hrough	6 weeks	Pure large K.-L.	0·5 c.c. in 2 days	Three families, all well.
(supposed ign body in nose)	3 weeks	Do.	0·5 c.c. in 1 day	Sisters. Father and mother = well.
None	3 weeks	Do.	0·5 c.c. in 3 days	
rly, but not really ill	5 weeks	Large K.-L. mixed	Died out in spite of agar plates and nearly pure culture	—
Do.	5 weeks	Do.	0·5 c.c. in 3 days	Four adults well; five children, one with sore throat.
ry slight	5 weeks	Large K.-L. pure	0·5 c.c. in 2 days	One child with sore nose; other children and mother = well; father said to have diphtheria.

(For report of the discussion on this paper, see ' Proceedings of the Royal Medical and Chirurgical Society,' Third Series, vol. xi, p. 4.)